PATENT
Attorney Docket No. 22903XA-T

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Joseph P. Steiner, et al.

Serial No.: not assigned

Filing Date: February 16, 2001

For: **SMALL MOLECULE PIPECOLIC ACID DERIVATIVE HAIR GROWTH COMPOSITIONS AND USES**

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Before action in the captioned application and before calculation of the filing fee, please amend the captioned application as follows:

IN THE SPECIFICATION

Please amend the specification by replacing the first sentence thereof with the following:

--This application is a divisional application of U.S. Patent Application Serial No. 09/089,373, filed on June 3, 1998, now U.S. Patent No. 6,191,125, granted February 20, 2001, the entire contents of which is incorporated by reference herein as though set forth in full.--

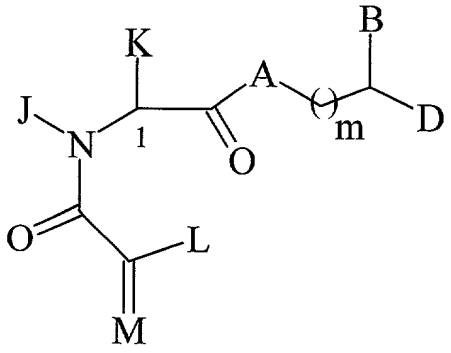
IN THE CLAIMS

Please cancel claims 1-4, which were allowed, as amended, in U.S. Patent Application Serial No. 09/089,373. Please cancel claim 7 without prejudice or disclaimer of the subject matter therein.

Please amend the claims as follows:

5. (Once amended) A pharmaceutical composition which comprises:

(i) an effective amount of a compound [pipecolic acid derivative] for treating alopecia or promoting hair growth in an animal in need thereof, wherein said compound is [the pipecolic acid derivative is a compound] of formula I



I

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

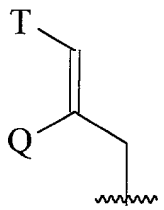
A is [CH_2,] O, NH, or N-(C_1-C_4 alkyl);

B and D are independently Ar, C_5-C_7 cycloalkyl substituted C_1-C_6

straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl, C_5-C_7 cycloalkenyl substituted C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl, or Ar substituted C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl,

wherein in each case, one or two carbon atom(s) of said alkyl or alkenyl [may be] is/are optionally substituted with one or two heteroatom(s) independently selected from the group consisting of oxygen, sulfur, SO, and SO_2 [in chemically reasonable substitution patterns],

or B and D are independently the fragment



wherein Q is hydrogen, C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl; and

T is Ar or C_5-C_7 cycloalkyl substituted at positions 3 and 4 with substituents independently selected from the group consisting of hydrogen, hydroxy, O-(C_1-C_4 alkyl), O-(C_2-C_4 alkenyl), and carbonyl;

Ar is selected from the group consisting of 1-napthyl, 2-

napthyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl and phenyl, monocyclic and bicyclic heterocyclic ring systems with individual ring sizes being 5 or 6 which [contain] have in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur, [;]

wherein Ar [contains] has 1-3 substituent(s) independently selected from the group consisting of hydrogen, halo, hydroxy, hydroxymethyl, nitro, CF_3, trifluoromethoxy, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, O-(C_1-C_4 straight or branched chain alkyl), O-(C_2-C_4 straight or branched chain alkenyl), O-benzyl, O-phenyl, amino, 1,2-methylenedioxy, carbonyl, and phenyl;

L is either hydrogen or U; M is either oxygen or CH-U, provided that if L is hydrogen, then M is CH-U, or if M is oxygen then L is U;

U is hydrogen, O-(C_1-C_4 straight or branched chain alkyl), O-(C_2-C_4 straight or branched chain alkenyl), C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_5-C_7 cycloalkyl, C_5-C_7 cycloalkenyl substituted with C_1-C_4 straight or branched chain alkyl or C_2-C_4 straight or branched chain alkenyl, (C_1-C_4 alkyl or C_2-C_4 alkenyl)-Ar, or Ar;

J is hydrogen, C_1 or C_2 alkyl, or benzyl; K is C_1-C_4 straight

or branched chain alkyl, benzyl or cyclohexylmethyl; or J and K are taken together to form a [5-] 7 membered heterocyclic ring which is substituted with oxygen, sulfur, SO, or SO_2;

[n] m is 0-3; and

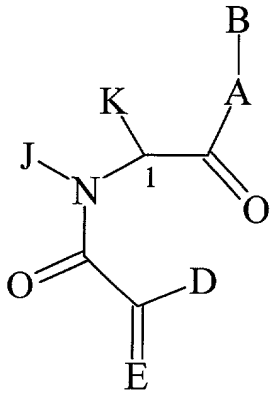
said [pipecolic acid derivative] compound has an affinity for FKBP-type immunophilins; [and]

(ii) a second hair revitalizing agent; and

(iii) a pharmaceutically acceptable carrier.

6. (Once amended) A pharmaceutical composition which comprises:

(i) an effective amount of a compound [pipecolic acid derivative] for treating alopecia or promoting hair growth in an animal in need thereof, wherein said compound is [the pipecolic acid derivative is a compound] of formula II

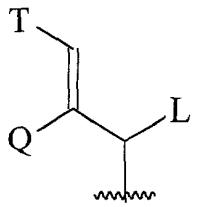


II

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A is O, NH, or N-(C_1-C_4 alkyl);

B is hydrogen, CHL-Ar, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_5-C_7 cycloalkyl, C_5-C_7 cycloalkenyl, Ar substituted C_1-C_6 alkyl or C_2-C_6 alkenyl, or



wherein L and Q are independently hydrogen, C_1-C_6 straight or branched chain alkyl, or C_2-C_6 straight or branched chain alkenyl; and

T is Ar or C_5-C_7 cyclohexyl substituted at positions 3 and 4 with substituents independently selected from the group consisting of hydrogen, hydroxy, O-(C_1-C_4 alkyl), O-(C_2-C_4 alkenyl), and carbonyl;

Ar is selected from the group consisting of 1-napthyl, 2-napthyl, 2-furyl, 3-furyl, 2-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, and phenyl, having 1-3 substituent(s) independently selected from the group consisting of hydrogen, halo, hydroxy, nitro, CF_3, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, O-(C_1-C_4 straight or branched

chain alkyl), O-(C_2-C_4 straight or branched chain alkenyl), O-benzyl, O-phenyl, amino, and phenyl; [.]

D is hydrogen or U; E is oxygen or CH-U, provided that if D is hydrogen, then E is CH-U, or if E is oxygen, then D is U;

U is hydrogen, O-(C_1-C_4 straight or branched chain alkyl), O-(C_2-C_4 straight or branched chain alkenyl), C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_5-C_7-cycloalkyl, C_5-C_7 cycloalkenyl substituted with C_1-C_4 straight or branched chain alkyl or C_2-C_4 straight or branched chain alkenyl, 2-indolyl, 3-indolyl, (C_1-C_4 alkyl or C_2-C_4 alkenyl)-Ar, or Ar;

J is hydrogen, C_1 or C_2 alkyl, or benzyl; K is C_1-C_4 straight or branched chain alkyl, benzyl or cyclohexylethyl; or J and K are taken together to form a [5-] 7 membered heterocyclic ring which is substituted with oxygen, sulfur, SO, or SO_2; and

said compound has an affinity for FKBP-type immunophilins;

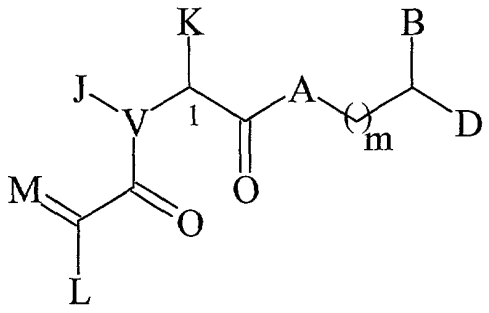
(ii) a second hair revitalizing agent; and

(iii) a pharmaceutically acceptable carrier.

8. (Once amended) A pharmaceutical composition which comprises:

(i) an effective amount of a compound [pipecolic acid derivative] for treating alopecia or promoting hair growth in an animal in need thereof, wherein said

compound is [the pipecolic acid derivative is a compound] of [formula] formula IV



IV

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

V is C, N, or S;

J and K, taken together with V and the carbon atom to which they are respectively attached, form a [5-] 7 membered saturated or unsaturated heterocyclic ring [containing] having, in addition to V, one or more heteroatom(s) selected from the group consisting of O, S, SO, SO_2, N, NH, and NR;

R is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_9 cycloalkyl [cycloakyl], C_5-C_7 cycloalkenyl, or Ar_1,

wherein R is either unsubstituted of substituted with one or more substituent(s) independently selected from the group consisting of halo, haloalkyl, carbonyl, carboxy, hydroxy, nitro, trifluoromethyl, C_1-C_6 straight or

branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, thioalkyl, alkylthio, sulfhydryl, amino, alkylamino, aminoalkyl, aminocarboxyl, and Ar_2;

Ar_1 and Ar_2 are independently an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring, [;]

wherein the individual ring size is 5-8 members, [;]

wherein said heterocyclic ring has [contains] 1-6 heteroatom(s) independently selected from the group consisting of O, N, and S;

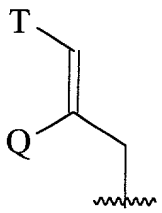
[A, B, D, L, M, and m are as defined in claim 5 above;]

A is O, NH, or N-(C_1-C_4 alkyl);

B and D are independently Ar, C_5-C_7 cycloalkyl substituted C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl, C_5-C_7 cycloalkenyl substituted C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl, or Ar substituted C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl,

wherein in each case, one or two carbon atom(s) of said alkyl or alkenyl is/are optionally substituted with one or two heteroatom(s) independently selected from the group consisting of oxygen, sulfur, SO, and SO_2,

or B and D are independently the fragment



wherein Q is hydrogen, C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl; and

T is Ar or C_5-C_7 cycloalkyl substituted at positions 3 and 4 with substituents independently selected from the group consisting of hydrogen, hydroxy, O-(C_1-C_4 alkyl), O-(C_2-C_4 alkenyl), and carbonyl;

Ar is selected from the group consisting of 1-napthyl, 2-napthyl, 2-furyl, 3-furyl, 2-thieny1, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl, and monocyclic and bicyclic heterocyclic ring systems with individual ring sizes being 5 or 6, which have in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur,

wherein Ar has 1-3 substituent(s) independently selected from the group consisting of hydrogen, halo, hydroxy, hydroxymethyl, nitro, CF_3, trifluoromethoxy, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, O-(C_1-C_4 straight or branched chain alkyl), O-(C_2-C_4 straight or branched chain

alkenyl), O-benzyl, O-phenyl, amino, 1,2-methylenedioxy, carbonyl, and phenyl;

L is either hydrogen or U; M is either oxygen or CH-U, provided that if L is hydrogen, then M is CH-U, or if M is oxygen then L is U;

U is hydrogen, O-(C_1-C_4 straight or branched chain alkyl), O-(C_2-C_4 straight or branched chain alkenyl), C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_5-C_7 cycloalkyl, C_5-C_7 cycloalkenyl substituted with C_1-C_4 straight or branched chain alkyl or C_2-C_4 straight or branched chain alkenyl, (C_1-C_4 alkyl or C_2-C_4 alkenyl)-Ar, or Ar; and

m is 0-3; [and]

(ii) a second hair revitalizing agent; and

(iii) a pharmaceutically acceptable carrier.

REMARKS

Upon entry of the above amendments, claims 5, 6, and 8 are pending in the application. Canceled claims 1-4 were allowed, as amended, in U.S. Patent Application Serial No. 09/089,373. The amendments do not introduce new matter within the meaning of 35 U.S.C. §132. Basis for the amendments is found at page 26, lines 5-9, as well as claims 5, 6, and 8 as originally filed, and elsewhere throughout the specification and claims. Accordingly,

the Examiner is respectfully requested to enter the above amendments before examination.

The Examiner is welcomed to telephone the undersigned attorney if (s)he has any questions or comments.

Respectfully submitted,

NATH & ASSOCIATES PLLC

Date: February 16, 2001

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